growth factor, leukemia inhibitory factor, membrane associated steel factor, and soluble steel factor; (2) selecting cells that have characteristics (a) and (b) above, and (3) isolating said human pluripotential cell; and wherein the characteristics of the cell include having a normal karyotype.

REMARKS

Claims 1-4 are pending. Claims 1 and 4 are amended herein. Attached as Appendix A is a marked-up version of the pending claims.

Applicants respectfully acknowledge withdrawal of the rejection under U.S.C. § 112, 1st paragraph, and the double patent rejection.

Claims 1-3 are rejected under 35 U.S.C. § 112 as allegedly indefinite. Specifically, the Office Action states that it allegedly is not clear what characteristics the claimed cells are required to have. Claim 1 as amended specifies that the cell has the potency characteristics of a cell derived from a primordial germ cell by a specific process. This potency and the process are taught throughout the specification. One skilled in the art, therefore, could produce the cells and then compare those cells to see if a cell has the same characteristics as taught by the specification and as specified in claim 1. The claim has also been amended to state that the common characteristics must include having a normal karyotype. Support for this amendment can be found in the specification on page 19, line 18. In view of this amendment, applicant requests reconsideration and withdrawal of the rejection of claims 1-3 under § 112, second paragraph.

The rejection of claim 4 under 35 U.S.C.§ 112, second paragraph, is maintained. The amendment of claim 4 as attempted in the Amendment dated January 3, 2000, which addressed this rejection, was not entered. Claim 4 is amended herein to delete the phrases "all" and "essentially." Furthermore, the claim has been amended to include the potency characteristics as noted above. In view of this amendment, the rejection under 35 U.S.C. §112, second paragraph, is believed to be rendered moot.

The Examiner has also maintained her refusal to grant priority to U.S. Patent No. 07/958,562, on the basis that "[t]here is no disclosure in the specification of 07/958,562 which enables non-murine pluripotent cells." The Office Action suggests that the method was enabled in the earlier specification but the product of the method allegedly was not. The Examiner maintains this rejection although the method of making the non-murine pluripotent cells, as disclosed in the 07/958,562 patent application, was proven successful for isolating non-murine pluripotent cells and although the 07/958,562 patent application, which issued as U.S. Patent No. 5,453,357, specifically specifies throughout that it provides "non-mouse pluripotential . . . cells." Furthermore, claim 9 of the issued patent is to a method of making pluripotential embryonic stem cells, wherein the stem cell is derived from a mammal, not limited to mouse. Given this language and the issued claims, it seems inconsistent to assert that the 07/958,562 application fails to enable non-murine pluripotent cells but does enable a method of making the non-murine pluripotential cells. The legal standard for enablement is whether the specification is sufficient to enable a person skilled in the art to *make* or *use* the invention. *See* 35 U.S.C. §112; *see also*

Atmel Corp. v. Information Storage Devices, Inc., 53 U.S.P.Q.2d 1225 (Fed. Cir. 1999). Thus, to enable non-murine pluripotential cells, the specification of the earlier application must teach a method of making and using the cells. More specifically, the specification must teach the skilled artisan how to make and use the invention without undue experimentation. *See Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997). In fact, a considerable amount of experimentation is permissible so long as it is merely routine or so long as the "specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed." *Ex parte Jackson*, 217 U.S.P.Q. 804, 807 (1982). Applicants already have provided evidence regarding how one skilled in the art could use the method taught in the 07/958,562 application to make pluripotential cells from non-murine sources without undue experimentation, and the Patent Office already has found the method of making non-murine pluripotential cells fully enabled in the 07/958,562 application. The Office Action does not clarify how a method of making a product can be fully enabled and yet fail to teach how to make the same product. The Office Action cites no legal support for this view. In view of the legal support to the contrary, applicants request withdrawal of the refusal to enter the claim to priority.

The Examiner has also maintained her rejection of claims 1-3 over Wheeler (U.S. Pat. No. 5,523,226). As stated above, applicants are entitled to claim priority to the 07/958,562 application, and Wheeler, therefore, is not prior art as to the present application.

The Examiner also cites Pera et al., Int. J. Cancer 40:334 (1987) and Notarianni et al., J. Reprod. Fert. Suppl. 41:51-56 (1990) as allegedly anticipating claims 1-4 and claims 1-3, respectively. As described above, however, claim 1 has been amended to specify that the cells have the characteristic of having a normal karyotye. The cells derived by Pera et al. are embryonal carcinoma (EC) cells which are derived from tumor cells and lack a normal karyotype. See Wright M. (1998) *Embryonic Stem Cells, Part One: History and Use*, Art to Science 17 (3):1-3 (characterizing undifferentiated, pluripotent cells derived from tetracarcinomas, EC cells, as having "an abnormal chromosome complement") (attached as Appendix B); see also, Sandberg et al. (1996) *Reviews of Chromosome Studies in Urological Tumors. III. Cytogenetics and Genes in Testicular Tumors*. J. Urol. 155:1531-56 (characterizing the abnormal karyotype of testicular germ cell tumors) (abstract attached as Appendix C). Thus, in view of this amendment, Pera et al. cannot anticipate the claimed cells. Applicants request withdrawal of the rejection of claims 1-3 in view of Pera et al.

Applicants also request reconsideration and withdrawal of the rejection in view of Notarianni et al. The cells described by Notarianni et al. lack the capacity to be maintained on feeder layers for at least 20 passages and still give rise to embryoid bodies and multiple differentiated cell phenotypes in monolayer culture. See Hong et al. (1998) *Production of medakafish chimeras from a stable embryonic stem cell line*, P.N.A.S. 95:3679-84 (citing Notarianni et al. but stating that, at least based on peer-reviewed, published journal articles as of 1998, the only stable embryonic cell lines that reportedly maintained pluripotency were murine

cells) (attached as Appendix D); see also, Wheeler (U.S. Patent No. 5,523,226), col. 2, lines 55-58 (stating that Notarianni et al. failed to "convincingly show that pluripotential embryonic stem cells were produced"). As claims 1 and 4 recite cells having the capacity to be maintained in culture and retain pluripotency, Notarianni cannot anticipate these independent claims or their respective dependent claims. The Federal Circuit has held that:

> A claim is anticipated only if each and every element *as set forth in the claim* is found, either expressly or inherently described, in a single prior art reference.

Constant v. Advanced Micro-Devices, Inc., 848 F.2d 1560, 1570 (Fed. Cir. 1988) (quoting *Kalman v. Kimberly Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983)) (emphasis in original). Applicant thus respectfully requests that the Examiner withdraw her Section 102(b) rejection of these claims.

Pursuant to the above remarks, allowance of the pending application is believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

A check for $1300.00 for a five-month extension of time ($945.00) and for a request for continued examination under 37 C.F.R. § 1.114 ($355.00) is enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as Express Mail Invoice EL403505220US in an envelope addressed to: Box RCE, Commissioner for Patents, Washington, D.C. 20231, on the date below.

Everardo McFarlane

2-28-01
Date